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INTEGRATED mFLUME RECONSTITUTION SYSTEM FOR BIOLOGICAL AND MEDICAL SUPPLIES

Integrated MEMS Delivery System for both Liquid and Reconstituted Drugs

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14. ABSTRACT
The overall goal of this project was to develop an integrated mFLUME system for the reconstitution, metering, and delivery of biological and medical supplies. This system would allow for the on-demand reconstitution of a wide range of medical supplies that have been stored in dry form for robustness, convenience, and shelf life. The MEMS system required the development and integration of micro-fluidic control components, including valves, pumps, mixing chambers, and fluid ejection ports, with dry material and solvent reservoirs and on-board electronic control systems. A fully integrated device for the reconstitution of a lyophilized drug was never created. However, under this contract, significant advances were made in the area of MEMS-based fluid control systems, including planar valves, mixers, pumps, and interconnects. In addition, integration of a working microFLUMES device into an injection-molded package was demonstrated under a contract extension. In addition, attention was brought to the MEMS community regarding micro-fluid mechanical processes, including the presence and effects of large momentum and scalar gradients.

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Final Report

Integrated mFLUME Reconstitution System for Biological and Medical Supplies

(Integrated MEMS Delivery System for both Liquid and Reconstituted Drugs)

Contract # F33615-97-1-2730

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University of California at Berkeley

The overall goal of this project was to develop an integrated μFLUME system for the reconstitution, metering, and delivering of biological and medical supplies. This system would allow for the on-demand reconstitution of a wide range of medical supplies that have been stored in dry form for robustness, convenience, and shelf life. The MEMS system required the development and integration of micro-fluidic control components, including valves, pumps, mixing chambers, and fluid ejection ports, with dry material and solvent reservoirs and on-board electronic control systems.

A fully integrated device for the reconstitution of a lyophilized drug was never created. However, under this contract significant advances were made in the area of MEMS-based fluid control systems including planar valves, mixers, pumps, and interconnects. In addition, integration of a working microFLUMES device into an injection molded package was demonstrated under a contract extension. In addition, attention was brought to the MEMS community regarding micro-fluid mechanical processes including the presence and effects of large momentum and scalar gradients. Specific developments are described below.

Micro-Fluidic Interconnects

As with integrated circuits, packaging for fluidic MEMS devices can be a major expense. Typically, connecting to the outside world has involved aligning and gluing tubes to holes etched in the device surface. This sort of manual alignment is both costly and difficult. Therefore, we developed integrated interconnects which connect microfluidic devices to each other and also to the macroscopic world.

Using our experience in the development of micro-needles, a new interconnection approach was developed to both connect μFLUME devices as well as providing an easy approach for fluid supply. The micro-needles are fabricated at the same time as the MEMS fluid control components. They can then be used to pierce membranes such as a vitamin capsule or membrane covering the port for another device.

Planar Micro-Valves

The work at Berkeley focused on the development of integrable, planar components because of the high development and manufacturing costs predicted for multi-layer MEMS devices. Initially we used gas-liquid interfaces to generate and control fluid motion using thermal phase changes. However, this approach required too much power for portable devices and had unexpected and

undesirable effects specifically in valves. Because of these issues, we developed micro-valves that contain moving parts fabricated *in situ*. Our approach used prebonded Silicon On Insulator (SOI) wafers in conjunction with Deep REI etching. Using this approach we developed under this contract, the first controlled planar micro-valves as well as the first micro check-valves with moving components.

Micro-pumps

Two different micro-pumps were developed under the contract. The first extended our approach of using phase change to create a positive-displacement pump. Positive displacement approach is ideal for MEMS devices because they are characterized by high head pressure, although they generally have low flow rates. However, these characteristics work extremely well for most MEMS applications. The check-valves provided the missing component because of their unique viscous-driven actuation as well as their extremely high pressure drop in the closed position. These devices have been demonstrated to work for over 12 hours continuously.

The second micro-pumps provide faster flow rates and are completely reversible. They use marangoni flows generated by small temperature gradients across a thermal or other bubble. While these devices do not generate high head pressure, they can generate high flow rates. Our initial prototypes used thermal bubbles because of their controllability. This was found to require significant power because the device heats up. An additional advantage is their ease of fabrication; only heaters are needed, without the need for moving parts.

Micro-pumps and Mixer

The first truly integrated MEMS fluidic device, a controlled micromixer, was developed under this contract. This device is entirely self-contained and only requires inputs and outputs for fluids and power. To make this micro-mixer, two positive displacement micro-pumps provide time-dependent flows into a channel. Because of the efficiency of the check-valves, the pumps demonstrated significant improvements over previous pumps.

Device Integration in an Injection Molded assembly

Under a contract extension, the micro-mixer was integrated into a plastic, injection-molded housing. This project was performed to investigate techniques to create hybrid devices as well as improving our ability to create fluidic interconnects.

Wetting and Flow Studies

For the drug delivery system, a quantity of freeze-dried drug must be attached from which doses can be taken and injected into the body. The original idea was to have a reservoir filled with the drug, an external pressurized water source connected at one end, and a connection to a MEMS mixing and injection device on the other. Shortly before the first injection, the reservoir would be flooded with water, which would quickly become saturated. A microvalve in the MEMS device would allow for small quantities of saturated solution to be drawn off. As each dose was removed, pure water would enter the reconstitution chamber. If the output volume flow rate were small enough, the incoming pure water would become saturated before exiting. Therefore, the output from the drug reservoir would remain saturated for many doses.

Reservoir Filling and Sealing

Significant work has been done to develop ways to improve sealing and filling of MEMS devices. The approaches were reported at the Second PI Meeting. These approaches included the use of patterned photoresist to seal micro-fluidic systems and the use of small channels that will allow air to escape from dead end passages.

In addition, we have designed procedures to implement epoxy in a device with electrical circuits and sealed flow structure. A proposed solution to the problems observed during the preliminary trials calls for fabricating the epoxy flow structure over electrical circuits and capped with a flat surface that is coated with unexposed epoxy. The unexposed epoxy should conform to the slight difference in the feature thickness and will then be exposed to properly seal the flow structure.

Interconnects and Seals

With the demonstration of sealed epoxy channel, we extended the concept to design a process that would produce sealed channels, fluid access ports, thermal isolation to key components and access to electrical through a batch process that may be more commercially viable. As an added benefit, the channels are optically transparent from all sides and could be valuable in flow visualization.

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